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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/522,341

01/25/2005

Michael Kock

12810-00057

5941

23416

7590

02/22/2008

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EXAMINER

ZHENG, LI

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

02/22/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/522,341	<b>Applicant(s)</b> KOCK ET AL.	
	<b>Examiner</b> LI ZHENG	<b>Art Unit</b> 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-34 is/are pending in the application.
- 4a) Of the above claim(s) 11-20 and 27-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-10,21-26 and 32-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. Claims 1 and 3-34 are pending.
2. Applicant's cancellation of claim 2, amendments to claims 1, 3-6, 10, 21-26, and submission of new claims 32-34 filed on 11/15/2007 are acknowledged and entered.  
  
Claims 11-20 and 27-31 are withdrawn for being drawn to non-elected inventions.  
  
Claims 1, 3-10, 21-26 and 32-34 are examined on the merits.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The objection to the specification is withdrawn due to specification amendment.

***Claim Objection***

5. The objections to claims 4-6 and 21-24 are withdrawn due to claim amendment.
6. New claims 32 and 33 are objected for being drawn to non-elected inventions.

***Claim Rejections - 35 USC § 112***

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7. Claims 1, 3-10, 21-26 remain rejected and new claims 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record stated in the Office action mailed May 31, 2007. Applicants traverse in the paper filed November 15, 2007. Applicants' arguments have been fully considered but were not found fully persuasive.

For claim 1:

Applicants argue claim 1 has been amended so that the rejections are rendered moot (response, page 16, 1<sup>st</sup> paragraph).

The Office contends that although claim 1 has been amended, the amended recitation, "marker protein capable of causing a toxic effect directly or indirectly", still renders the claim indefinite. It is unclear what the recitation encompasses. The metes and bounds are not clear. It is suggested to delete the recitation "capable of ". Further, the amended recitation, "an expression cassette or expression cassettes ensuring expression of said double-stranded marker protein ribonucleic acid sequence", still renders the claim indefinite. It is unclear what the recitation encompasses. The recitation still reads on any expression cassette that causes expression of double-stranded marker protein. It is suggested to further amend the claim to recite that those expressing cassettes directly express said double-stranded marker protein ribonucleic acid sequence.

***Written Description***

8. Claims 1, 3-4, 7-10 and 25-26 remain and claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed May 31, 2007. Applicants traverse in the paper filed November 15, 2007. Applicants' arguments have been fully considered but were not found fully persuasive.

Applicants argue that the Office has not provided sufficient evidence to rebut the presumption of adequacy of a description to a process using marker protein and double-stranded marker protein ribonucleic acids and that claims 5-6 recite seventeen marker protein and 24 sequences which can be used in the process and constitute a representative number of species in claimed genus (response, page 18, 2<sup>nd</sup> paragraph).

The Office contends that the for most of those seventeen candidate marker proteins and their corresponding toxic compounds, neither the specification nor the prior art provide guidance on whether those claimed "toxic compounds" are actually toxic to plant cell under the condition used for transformation in presence of corresponding marker proteins. No guidance are provided as to what the minimum concentration of compounds used for selection for plant transformation is and whether such concentration is practically feasible or not given that any given compound could become toxic to cells at very high concentration. Therefore, the specification does not correlate those marker

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proteins with the function of being able to be used for selection in plant transformation.

Even though seventeen candidate proteins are provided, it is unclear whether they belong to the claimed genus or not.

### *Enablement*

9. Claims 1, 3-4, 7-10 and 25-26 remain and claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the CodA marker protein and the dsRNA of CodA, does not reasonably provide enablement for any marker proteins capable of causing directly or indirectly a toxic effect for plant cells by any means, or any protein capable of converting any substance X that is nontoxic for said population of plant at any condition to a substance Y which is toxic for said population at any condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims, for the reasons of record stated in the Office action mailed May 31, 2007. Applicants traverse in the paper filed November 15, 2007. Applicants' arguments have been fully considered but were not found fully persuasive.

Applicants argue that the specification provides detailed description and guidance regarding at least seventeen specific marker proteins which can be used in the claimed process and that there is no undue experimentation involved in practicing the invention (response, the paragraph bridging pages 19-20; also page 20, 3<sup>rd</sup> paragraph).

The Office contends the instant claims read on any marker protein capable of causing directly or indirectly a toxic effect for plant cells by any means. The

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specification does not provide sequence information required for all the marker genes, except for the ones described in the specification . Even for those seventeen known genes described in specification except for CodA, no guidance or examples are provided in term of whether those genes encoding marker proteins function in plants, or what the concentration of substance X should be when used for selection etc. Even if they are functional in plants, it is unclear whether the silencing effect for a given marker gene is strong enough so that toxic compound is no longer produced by mark protein, which allows the negative selection. Further, if a plant cell expressing any marker protein which causes any toxic effect at any condition, which results in the death of the plant, it is practically difficult, if possible at all, to obtain such plant cell and use it for practicing the invention. Therefore, in the absence of further guidance, in contrast to Applicants' conclusion, undue experimentation would be required by one skilled in the art to practice the invention using any marker proteins.

Applicants further argue that the specification provides detailed description and guidance regarding seventeen marker protein and 24 sequences which can be used in the process and constitute a representative number of species in claimed genus (response, page 19, last paragraph).

The Office contends that those description and guidance are not enough to enable the claimed invention for the same reason as discussed above in the written description rejection.

***Claim Rejections - 35 USC § 103***

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10. Claims 1, 3-10 and 21-26 remain rejected and claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maliga et al. (March 29, 2001, WO 01/21768) in view of Smith et al. (2000, *Nature*, 407:319-320) and Applicants' admitted prior art, for the reasons of record stated in the Office action mailed May 31, 2007. Applicants traverse in the paper filed November 15, 2007. Applicants' arguments have been fully considered but were not found fully persuasive.

Applicants argue that Maliga et al. describe using expression of codA for selection whereas the instant invention describes using silencing of codA for selection (response, the paragraph bridging pages 21-22).

The Office contends that in the same paragraph of Applicants' response, Applicants clearly acknowledged that Maliga et al. teach lacking codA could be readily identified by 5-FC resistance. In addition, using codA as negative selection is well known in the plant transformation art.

Applicants further argue that the alleged motivation lacks specificity to support a legal conclusion of obviousness and that based on a teaching requiring expression of a marker protein for selection in a site specific recombination method to remove heterologous sequences from the plastid genome, one of ordinary skill in the art would not look to a reference disclosing gene silencing (response, page 22, last paragraph).

The Office contends that given the teaching that lacking codA expression can be readily used for a negative selection, it would have been obvious for a person with ordinary skill in the art to choose from a finite number of known methods to reduce or eliminate the expression of codA. For example, it would have been obvious for a person with ordinary skill in the art to try using homologous recombination to remove the codA

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from the genome. Alternatively, given the teaching of Smith et al., it would also have been obvious to try using hairpin silencing construct to reduce the expression of codA gene.

Applicants further argue that the proposed modification to Maliga et al requires a substantial reconstruction and redesign of element and change the principle under which Maliga et al operate and that introducing the construct of Smith et al. into the method of Maliga et al would render it inoperable (response, page 23, 1<sup>st</sup> paragraph).

The Office contends that introducing the hairpin construct of Smith et al. targeting codA, into the method of Maliga et al would function as expected to reduce or eliminate the expression of codA gene and renders the plant resistant to 5-FC compound. The Office also contends that the motivation do not have to come from the reference of Maliga et al. The motivation for instant rejection is derived from the general knowledge of a person with ordinary skill in the art.

Applicants further argue that Maliga et al and smith et al do not suggest the specific steps of the selection method as claimed.

The Office contends that in the specification the Applicants disclose that positive (such as npt, hph genes) and negative selection markers (including codA of SEQ ID NO: 2) and compounds used for selections are well known in the art and references are cited (specification, pages 1-3). A person with ordinary skill in the art would have the knowledge that double selection would be more effective to select true transformants as the false positive transformants escaped from the negative selection are unlikely to escape from a second selection with different mode of action.

*Summary*

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stuart F. Baum/

Primary Examiner, Art Unit 1638